

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 36, 37, 40, 41, 43, 44, 46-49, 58 and 59 are pending in the application, with claim 36 being the sole independent claim. Claim 36 is sought to be amended. Support for the amendment to claim 36 can be found throughout the specification, for example, at page 15, lines 10-15 and at page 17, lines 6-17. It is respectfully requested that the foregoing amendments be entered and considered.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***I. Claim Rejections Under 35 U.S.C. § 112, First Paragraph***

Claims 36, 37, 40, 41, 43, 44, 46-49 and 58 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. *See* Office Action, page 2. Applicants respectfully traverse this rejection.

The currently presented claims are directed to methods for identifying a compound that has the activity of inhibiting sister chromatid separation in eukaryotic cells. The methods comprise, *inter alia*, incubating with a test compound a separin in the presence of a

separin substrate. Importantly, independent claim 36 in its present form specifies that the substrate is a peptide or polypeptide comprising an amino acid sequence EXXR, wherein X is any amino acid, and the substrate is capable of being cleaved by the separin.

The written description rejection is based on the Examiner's position that the claims "are directed toward a genus of methods for identifying separin inhibitors using *any substrate*." Office Action, page 2 (emphasis added). According to the Examiner:

The claims encompass[] a highly variant genus of substrates with widely differing structural, chemical, and physical characteristics. The genus is highly variable because a significant number of structural differences between genus members is permitted.

While the specification discloses a human SCC1 protein substrate consisting of the amino acid sequence of SEQ ID NO: 1, the claims also encompass fragments or variants thereof which have structural, chemical, and physical characteristics that are different from the disclosed protein substrate consisting of the amino acid sequence of SEQ ID NO: 1. The specification does not provide a written description for these fragments or variants of SEQ ID NO: 1 which can be used in the claimed method.

Office Action, pages 2-3. Applicants respectfully disagree with the Examiner's assessment.

To satisfy the written description requirement of 35 USC § 112, first paragraph, an Applicant must convey with reasonable clarity to those skilled in the art that, as of the effective filing date, the Applicant was in possession of the invention. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). The written description requirement for a claimed genus can be satisfied by, e.g., disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure. *See Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *see also, Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324 (Fed.

Cir. 2002). In addition, the USPTO's guidelines indicate that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. *See M.P.E.P. § 2163*. The USPTO's guidelines note that "[w]hat constitutes a 'representative number' is an inverse function of the skill and knowledge in the art." *See Id.*

Contrary to the Examiner's assertion, the present specification describes numerous separin substrates -- in addition to SEQ ID NO: 1 -- that can be used in the methods of the invention. Other exemplary separin substrates disclosed in the specification include:

- Yeast Scc1 (specification, page 4, lines 3-5);
- N- and C-terminally tagged variants of yeast Scc1 containing either HA or Myc epitopes (specification, page 6, lines 3-16 and page 28, lines 4-12);
- HA-tagged variants of yeast Scc1 containing either an R268D mutation or an R180D mutation (the *single* mutations were shown to be cleaved by separin) (specification, page 7, lines 19-31 and page 8, lines 5-21);
- An Scc1 variant containing the FLAG epitope, the yeast VMA intein, and a chitin binding domain (specification, page 31, lines 1-14);
- Phosphorylated and unphosphorylated variants of Scc1 (specification, page 10, lines 7-10);
- Rec8, an Scc1 homolog that replaces Scc1 in the cohesin complex of meiotic cells and that was also shown to be cleaved by separin (specification, page 11, lines 14-29);
- Human SCC1 (specification, page 13, lines 8-25);

- A Myc-tagged variant of human SCC1 (specification, page 14, line 14, through page 15, line 2);
- N- and C-terminal deletion variants of human SCC1 (used to identify the sequence EXXR as the cleavage site) (specification, page 15, lines 3-15); and
- Rad21, an *S. pombe* homolog of Scc1 (specification, page 18, lines 10-13).

At the time of the effective filing date of the present application, the level of skill and knowledge in the art relating to the production of polypeptide fragments and variants having a specified activity was very high. Exemplary techniques that could have been used to produce separin substrate variants are outlined in the specification at page 20, lines 1-12. In view of the high level of skill and knowledge in the art, the numerous exemplary separin substrates disclosed in the specification would clearly be regarded as a representative number of species.

Applicants also note that the specification identifies the sequence motif EXXR as being "conserved in many SCC1 homologs in different species." See specification at page 15, lines 10-15. Given this consensus sequence and the other exemplary separin substrates described in the specification, a person of ordinary skill in the art, using routine molecular biological techniques, could easily design and express an almost infinite array of separin substrates. A person of ordinary skill in the art, in view of the present specification, would recognize that any peptide or polypeptide sequence containing an EXXR consensus sequences would serve as an adequate separin substrate for use in the present invention.

In addition, Applicants respectfully assert that the Examiner's comments regarding the "widely differing structural, chemical, and physical characteristics" of separin substrates is incorrect. As indicated in the specification, separin substrates are structurally and functionally related: The important functional characteristic shared by all separin substrates is that, by definition, they are cleaved by separin. This functional characteristic is directly correlated with the common structural characteristic shared by separin substrates, namely the cleavage sequence EXXR. *See* specification at page 15, lines 3-24. These structural and functional attributes of separin substrates are specified in currently presented independent claim 36. Thus, the separin substrates used in the practice of the currently claimed methods do not have "widely differing structural, chemical, and physical characteristics" as asserted by the Examiner.

In view of: (a) the large number of separin substrates that are disclosed in the specification and that were known in the art; (b) the fact that all separin substrates share the same structural attributes which allow these polypeptides to be cleaved by separin; and (c) the ability of persons of ordinary skill in the art to easily construct additional separin substrates based on the substrates disclosed in the specification, a person of ordinary skill in the art would conclude that Applicants were in possession of the full scope of methods encompassed by the present claims.

Finally, Applicants note that claim 58 specifies that the substrate is human SCC1. Thus, the Examiner's rationale for the rejection does not apply to claim 58.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

**II.      *Claim Rejections Under 35 U.S.C. § 112, Second Paragraph***

Claims 36, 37, 40, 41, 43, 44, 46-49, 58 and 59 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting essential steps, such omission amounting to a gap between the steps. *See* Office Action, page 3. Applicants respectfully traverse this rejection.

This rejection is based on the Examiner's position that "[t]he claims do not recite steps that show how the inhibiting effect of the test compound inhibits sister chromatid separation in eukaryotic cells." *See* Office Action, page 3. Applicants believe that the previously presented claim language would be clearly understood by persons of ordinary skill in the art and would not be regarded as "omitting essential steps." It is clear from the specification that the proteolytic activity of separin is necessary for chromatid separation. *See, e.g.*, specification at page 4, lines 1-5 (and reference cited therein), and page 7, lines 10-12. Therefore, a compound that inhibits the proteolytic activity of separin necessarily inhibits chromatid separation.

Nevertheless, for purposes of expediting allowance of the present application, Applicants have amended claim 36 to specify that the compound determined in (b) to inhibit the proteolytic activity of the separin has the activity of inhibiting sister chromatid separation in eukaryotic cells. In view of this amendment, Applicants believe that the rejection under 35 U.S.C. § 112, second paragraph, has been fully accommodated and should be withdrawn.

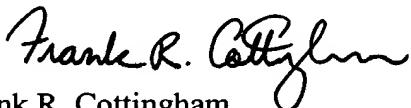
***Conclusion***

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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